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Progress towards a multi-modal capsule endoscopy device featuring microultrasound imaging

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Abstract—Current clinical standards for endoscopy in the gastrointestinal (GI) tract combine high definition optics and ultrasound imaging to view the lumen superficially and through its thickness. However, these instruments are limited to the length of an endoscope and the only clinically available, autonomous devices able to travel the full length of the GI tract easily offer only video capsule endoscopy (VCE). Our work seeks to overcome this limitation with a device (“Sonopill”) for multimodal capsule endoscopy, providing optical and microultrasound (μ US) imaging and supporting sensors¹.

μ US transducers have been developed with multiple piezoelectric materials operating across a range of centre frequencies to study viability in the GI tract. Because of the combined constraints of μ US imaging and the low power / heat tolerance of autonomous devices, a hybrid approach has been taken to the transducer design, with separate transmit and receive arrays allowing multiple manufacturing approaches to maximise system efficiency. To explore these approaches fully, prototype devices have been developed with PVDF, high-frequency PZT and PMN-PT composites, and piezoelectric micromachined ultrasonic transducer arrays. Test capsules have been developed using 3D printing to investigate issues including power consumption, heat generation / dissipation, acoustic coupling, signal strength and capsule integrity. Because of the high functional density of the electronics in our proposed system, application specific integrated circuits (ASICs) have been developed to realise the ultrasound transmit and receive circuitry along with white-light and autofluorescence imaging with single-photon avalanche detectors (SPADs).

The ultrasound ASIC has been developed and the SPAD electronics and optical subsystem have been validated experimentally. The functionality of various transducer materials

has been examined as a function of frequency and ultrasound transducers have been developed to operate at centre frequencies in the range 15 - 50 MHz. *Ex vivo* testing of porcine tissue has been performed, generating images of interest to the clinical community, demonstrating the viability of the Sonopill concept.

Keywords—endoscopy; microultrasound; prototyping; pre-clinical; capsules

I. INTRODUCTION

Video capsule endoscopy (VCE) is a maturing field which has established itself as a useful tool in the diagnosis of small bowel disorders [1] and other diseases of the human gastrointestinal tract (GIT). Based on its successful uptake into clinical practice, there has been wide research into methods to expand its functionality in the diagnosis of GIT disease [2], [3]. One current limitation is that optical imaging functionality allows only surface observation, with sub-surface examination still requiring conventional endoscopic ultrasound (EUS) and thus being difficult in the small bowel. This paper presents progress towards ultrasound capsule endoscopy (USCE). The work it presents has focused on the development of microultrasound (μ US) transducers, prototype capsules for pre-clinical testing and the electronics necessary for miniaturised multi-modal sensing.

II. MICROULTRASOUND TRANSDUCERS

The layers of the human GIT are relatively thin (1 - 2 mm) with respect to normal ultrasound (US) imaging wavelengths and frequencies [4], making US / μ US in the 15 - 50 MHz range best suited for USCE applications. Previous work has shown that it can allow differentiation of the layers of the GIT [4] as well as quantitative analysis of diseased tissue [5].

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Designing μ US transducers for USCE places unusual constraints on the physical and electronic complexity of the entire system because of the limited internal dimensions. For this reason, the transmitting and receiving transducers in the Sonopill are separated, with the transmitter used in a monolithic, unfocused mode. This allows the transmitting electronics to be reduced to a single channel, as well as eliminating the need for transmit/receive switches. An additional, beneficial side-effect of the separation of the transmitting and receiving transducers is that they can have completely different acoustic stacks, allowing freedom in material selection normally reserved for pitch-catch applications. Multiple possible piezoelectric materials and their different forms and configurations have been considered, with attention on maximizing both transmit and receive efficiency while maintaining ease of manufacturing.

A. Materials

Piezoelectric composites are common in commercial ultrasound imaging systems, as changing the volume fraction of the bulk piezoelectric material in the piezocomposite allows the mechanical and piezoelectric properties to be tailored. Piezocomposites can provide high electromechanical coupling coefficient (e.g. k_t of PMN-PT 1-3 composite can reach 0.9 [6]) and reduced acoustic impedance for better energy transmission into the load medium. Moreover, mechanical flexibility and formability can be achieved from compositing stiff and fragile piezomaterials (e.g. PZT and relaxor-PT single crystals) with flexible polymer matrix. The resulting high performance makes these materials suitable for both transmit and receive arrays. However, they can be more difficult to manufacture.

Piezoelectric polymers, e.g. polyvinylidene fluoride (PVDF), are attractive in fabricating flexible devices and devices with large curvatures. Their high piezoelectric stress constants and low elastic stiffness give them advantages in producing high sensitivity receivers, but their low d_{33} reduces their usability in ultrasound transmitters [7]. Their relatively high g_{33} , however, makes them a viable candidate for the receive transducer in the capsule.

Finally, capacitive and piezoelectric micromachined ultrasound transducers (CMUTs and PMUTs) gain attention because of their advantages over conventional fabrication technologies, including miniaturization, low acoustic impedance, high bandwidth and sensitivity, and their potential for wafer-scale production and integration with front-end electronics [8]. These advantages put them in a good position for the development of miniaturized ultrasonic devices. However, the complexity in establishing reliable manufacturing makes them a longer term consideration compared to more established methods.

B. Performance

To assess the performance of the different materials, a selection of transducers were tested for insertion loss and bandwidth and scans were obtained of a 10-wire test phantom with 10 μ m tungsten wires placed at 1 mm depth intervals to assess axial and lateral resolution (Fig.1). The resolution of the phantom images and the overall signal to noise were used to

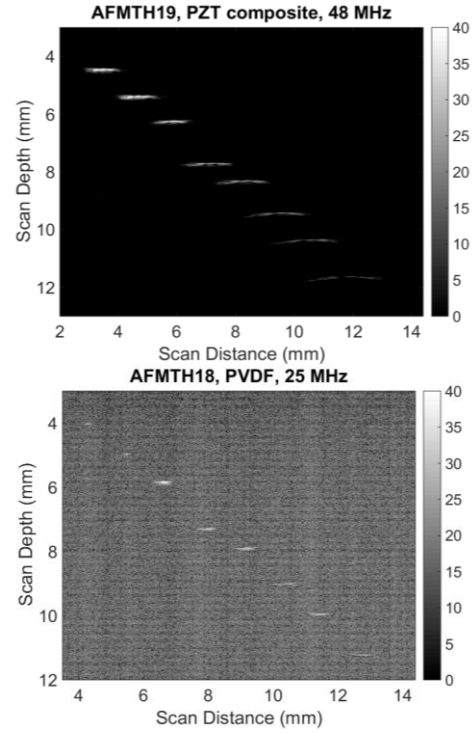


Fig.1 Wire target phantom images for AFMTH19 (48 MHz, PZT composite, above) and the AFMTH18 (23 MHz, PVDF, below) showing resolution and sensitivity for the two transducers.

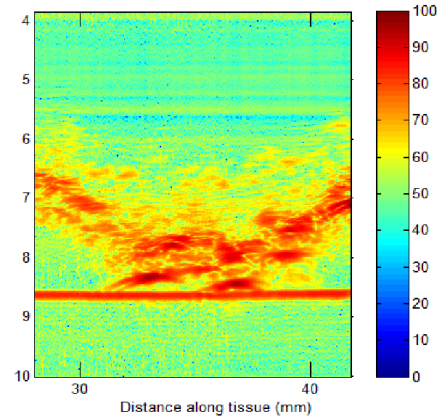


Fig.2 Microultrasound image of bowel tissue scanned with a 48 MHz focused, single-element transducer (AFMTH19)

determine the best transducer for imaging. This transducer (AFMTH19, 48 MHz, AFM Ltd, Birmingham, UK) was then used to obtain scans of porcine bowel and esophageal tissue sourced from an abattoir (Fig.2).

III. PROTOTYPE CAPSULES

A. Thermocap

Two of the core questions often raised in considering a medical capsule with high electronic complexity are power limits and thermal considerations. To address these concerns, a prototype capsule ("Thermocap") has been developed to

establish limits for the power that can safely be applied in a steady state and dynamic manner as well as the resulting thermal profile in and outside the capsule during *in vivo* testing.

The Thermocap is a 30 mm long x 10 mm diameter additively manufactured capsule (Verowhite, Objet Connex 500, Stratasys, Eden Prairie, USA) containing two miniature printed circuit boards (PCBs), fourteen thermistors, two voltage regulators, a humidity sensor and a power resistor. The capsule has been designed with integrated thermistor mounting holes spaced uniformly around the circumference and along the lateral axis to obtain a full temperature profile around it under different power and fluid flow conditions (Fig.3, left). An isolated power line allows precise control of the current to the power resistor and the humidity sensor allows continuous monitoring of the overall hermeticity of the capsule shell. Thermocap will be sealed with biocompatible epoxy and coated in parylene prior to use in a porcine model.

B. Sonocap

While there have been recent developments in research into ultrasound imaging in a capsule format [9], little information exists in the literature on the amount of direct or fluid-mediate tissue contact with the surface of the capsule that can be expected during passage. To investigate this and the resulting effect on the coupling of ultrasound waves into the media, a second capsule (“Sonocap”) has been designed to house four single-element μ US transducers and supporting electronics.

The Sonocap has the same manufacturing process and dimensions as the Thermocap, and the same steps are taken for biocompatibility. However, instead of thermistor mounts, it features four ultrasound transducers, three along the long axis and one at a 180° rotation from the others at the front of the capsule. A custom PCB within the capsule houses a 4-channel T/R switch (MD0101, Microchip Technology, Chandler, USA) and a 4-channel low noise amplifier (LNA) (ADA4807, Analog Devices, Norwood, USA) (Fig. 3 right).

IV. INTEGRATED ELECTRONICS

The heart of the capsule is a mixed-signal complementary metal oxide silicon (CMOS) application specific integrated circuit (ASIC). This will implement US transmit array pulse drivers and receive array amplifiers, a fast analog-digital converter (ADC) and buffering for digitized backscatter images. An embedded processor will provide addressing and control for US, autofluorescence and pH sensor arrays, and a finite state machine will transmit acquired image data serially over a tether or in a wireless implementation to a base station.

A. Ultrasound Analog Front-End

A major concern with the design of the US ASIC circuitry is the high capacitance inherent in some ultrasound transducers and its impact on the bandwidth of the receive amplifiers. To assess the necessary specification for the US front-end receiver, a commercial chip (AD8331, Analog Devices, Norwood, USA) was obtained with controllable input resistance and paired with a PVDF transducer. The input impedance of the amplifier was

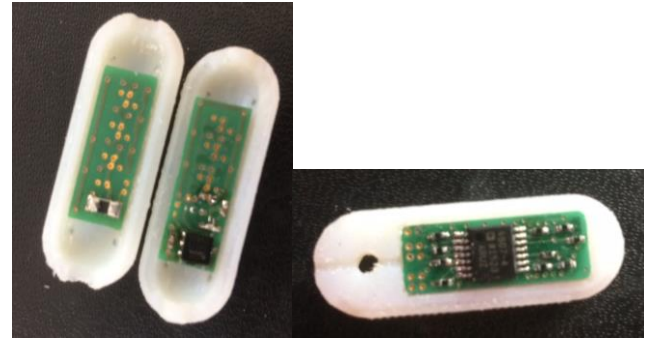


Fig.3 Thermocap (left) and Sonocap (right) with custom PCBs. Thermistor placement can be seen above and below the Thermocap PCBs, while the uppermost ultrasound transducer placement can be seen above the Sonocap PCB.

adjusted to 5 different values, and the resulting effect on the pulse was observed in the time and frequency domains (Fig.4).

B. Fluorescence Imaging

Fluorescence imaging (FI) is a valuable scientific and medical technique whose uses include diagnosis of disease within the GIT. Current FI systems are limited by physical bulk and power consumption and are thus not suitable for capsule endoscopy. Previous work has shown the viability of a miniaturised low-powered wireless FI capsule compact enough to examine the entire GIT, and exhibiting sufficiently low power consumption to operate from internal batteries over its entire journey through the GIT [10].

The capsule comprises a CMOS single photon avalanche detector (SPAD) imaging array and miniaturised optical isolation, controller, wireless communication and a data logging system. The capsule both induced and detected autofluorescence in intestinal disease phantoms. We also demonstrated the possibility of using endogenous fluorophores such as fluorescein isothiocyanate (FITC) as labelling

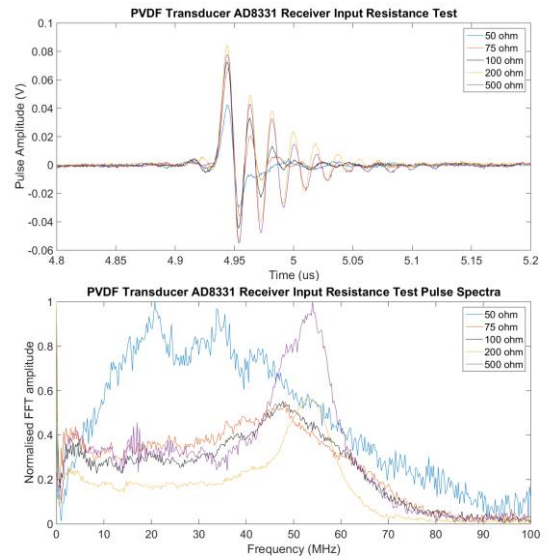


Fig.4 Through transmission pulse (above) and pulse spectra (below) with matched 30 MHz PVDF transducers and AD8331 front-end analog electronics

markers on mammalian tissue. Further miniaturisation will be achieved through reduction of optical component sizes and integration of the SPAD control with the overall system control ASIC.

C. pH sensing

With recent developments in microelectronics, solid-state sensors such as ion-sensitive field-effect transistors (ISFETs) have been developed and are finding uses in implantable diagnostic devices. We have demonstrated an array of 256 x 256 ISFET sensors (total area 4.6 mm x 4.7 mm) that was fabricated in a commercial foundry (Austria Microsystems, Premstaetten, Austria) using the standard 0.35 μm , four metal process [11]. The chip can detect pH levels from 2 to 12 with sensitivity up to 50mV/pH and very low drift of 0.8mV/hour. The results obtained from the chip are encouraging and fit with the psychosocial range that is suitable for use for pH in a capsule. However, a smaller chip die version of the previous work has to be implemented in order to fit the size-constrained multimodality pill.

V. DISCUSSION AND CONCLUSIONS

Current developments in the ultrasound transducer and electronics aspects of the Sonopill programme have produced promising initial results, suggesting the continued viability of the CEUS device in development. *Ex vivo* imaging of porcine bowel and oesophageal samples show good tissue layer differentiation and quantitative approaches have shown statistical significance between healthy and diseased murine tissues.

Prototype capsules have been successfully developed to test critical clinical concerns regarding safe operating limits and expected μUS signal quality and reliability in an *in vivo* environment. Ethical approval has been obtained for these trials and they are scheduled for the near future.

Electronic development is well under way, and the auto-fluorescence and pH sensing components have been successfully developed and tested. Testing of a commercial analog front-end chip has also shown that resistive impedance matching is not helpful for high capacitance transducers and can negatively affect the bandwidth of the system. Thus, the specifications for the final ultrasonic receive analog front-end have been established and ASIC development is showing excellent progress.

Overall, key findings have shown continuing viability of the USCE concept and the currently planned pre-clinical

testing should establish critical operation standards and possibilities.

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REFERENCES

- [1] U. C. Ghoshal, "Capsule Endoscopy: A New Era of Gastrointestinal Endoscopy," in *Endoscopy of GI Tract*, S. Amornytin, Ed. InTech, 2013.
- [2] G. Ciuti, A. Menciassi, and P. Dario, "Capsule Endoscopy: From Current Achievements to Open Challenges," *IEEE Rev. Biomed. Eng.*, vol. 4, pp. 59–72, 2011.
- [3] Z. Fireman, "Capsule Endoscopy: Future Horizons," *World J. Gastrointest. Endosc.*, vol. 2(9), pp. 305–7, 2010.
- [4] S. Ødegaard, L. B. Nesje, O. D. Lærum, and M. B. Kimmey, "High-frequency ultrasonographic imaging of the gastrointestinal wall," *Expert Rev. Med. Devices*, vol. 9, no. 3, pp. 263–273, May 2012.
- [5] A. Fatehullah, S. Sharma, I. P. Newton, A. J. Langlands, H. Lay, S. A. Nelson, R. K. McMahon, N. McIlvenny, P. L. Appleton, S. Cochran, and I. S. Näthke, "Increased variability in ApcMin/+ intestinal tissue can be measured with microultrasound," *Sci. Rep.*, vol. 6, p. 29570, Jul. 2016.
- [6] Z. Qiu, Y. Qiu, C. E. M. Demore, and S. Cochran, "Implementation of a PMN-PT piezocrystal-based focused array with geodesic faceted structure," *Ultrasonics*, vol. 69, pp. 137–143, Jul. 2016.
- [7] F. S. Foster, K. A. Harasiewicz, and M. D. Sherar, "A history of medical and biological imaging with polyvinylidene fluoride (PVDF) transducers," *IEEE Trans. Ultrason. Ferroelectr. Freq. Control*, vol. 47, no. 6, pp. 1363–1371, 2000.
- [8] Y. Qiu, J. V. Gigliotti, M. Wallace, F. Griggio, C. E. M. Demore, S. Cochran, and S. Trolrier-McKinstry, "Piezoelectric Micromachined Ultrasound Transducer (PMUT) Arrays for Integrated Sensing, Actuation and Imaging," *Sensors*, vol. 15, no. 4, pp. 8020–8041, Apr. 2015.
- [9] J. H. Lee, G. Traverso, C. M. Schoellhammer, D. Blankschtein, R. Langer, K. E. Thomenius, D. S. Boning, and B. W. Anthony, "Towards wireless capsule endoscopic ultrasound (WCEU)," in *Ultrasonics Symposium (IUS), 2014 IEEE International*, 2014, pp. 734–737.
- [10] M. A. Al-Rawhani, J. Beeley, and D. R. S. Cumming, "Wireless fluorescence capsule for endoscopy using single photon-based detection," *Sci. Rep.*, vol. 5, p. 18591, Dec. 2015.
- [11] B. C. Cheah, A. I. Macdonald, C. Martin, A. J. Streklas, G. Campbell, M. A. Al-Rawhani, B. Nemeth, J. P. Grant, M. P. Barrett, and D. R. S. Cumming, "An Integrated Circuit for Chip-Based Analysis of Enzyme Kinetics and Metabolite Quantification," *IEEE Trans. Biomed. Circuits Syst.*, vol. 10, no. 3, pp. 721–730, Jun. 2016.